

FTS-CDC-PHPPO

October 20, 2004
12:00 p.m. CDT

Coordinator The call is about to begin. We do appreciate everyone's patience for today's Select Agent teleconference call. Today's conference call is also being recorded for Net replay purposes. Any objections, you may disconnect at anytime. Today's conference call, there will be a Q&A session.

Let me introduce our first presenter for today's conference call, Ms. Susan Shiflett, you may begin when ready.

S. Shiflett Good day. Welcome to the 2004 Public House Teleconference Series on Infectious Disease. This is Susan Shiflett, Laboratory Training Coordinator in the Office of Public Health Preparedness at the Michigan Department of Community Health in Lansing, Michigan. Today's teleconference is being hosted by the Michigan Department of Community Health and is sponsored by the National Laboratory Training Network in

cooperation with the State Public Health Laboratories. Welcome to our Teleconference Select Agent Rule Update.

After the program, each participant needs to register and complete an evaluation form. Documenting your participation helps us to continue to bring high quality training programs in a variety of format. To do this, you need to go to the Web site <http://www.phppo.cdc.gov//phtnonline/> and the password is select. When you have completed the registration and evaluation form, you will be able to print your CEU certificate. You will have until November 20th to complete this process. These instructions are in your original confirmation letter and in the general handout. They were also e-mailed to each site representative this morning.

If time permits at the end of today's program, it will be opened up for questions. You are in a listen-only line. We cannot hear you. You can only hear us. Again, welcome and thank you for joining us. We have 59 sites today from across the United States listening to this teleconference.

Today's speaker is Dr. Charles Brokoff. Charles Brokoff is the Director of the CDC Select Agent Program. Prior to moving to Atlanta in August, he was the Director of the Division of Epidemiology and Laboratory

Services for the Utah Department of Health. He has also been in the Public Health laboratory director in Oregon and Idaho. He has degrees in the University of Wisconsin where he got his BS in Biology and a BS in Medical Technology, and the University of North Carolina where he received his MPH and DrPH. His 30 years in public health have primarily been at the state level, where he has worked closely with many local, state, federal, and private, public health and environmental organization. It is my pleasure to introduce to you and to welcome our speaker, Dr. Brokoff.

Dr. Brokoff

Thank you, Sue. I appreciate this opportunity to talk with you today about the Select Agent Program. In this presentation, I will provide an overview of the CDC regulation 42 CFR Part 73 also known as the Select Agent Rule. We'll also describe how the federal agencies, primarily CDC, USDA and Department of Justice are working together to implement this program.

Slide two: The CDC Select Rule had its origin in the year 1995 when a number of events occurred that caused congress and the federal government to review existing federal regulations restricting the acquisition of biological agents and toxins. It was noted that for some

human pathogens, there were no licensing or registration requirements for entities that are transferring these agents within the United States.

Nobody really knew who had these agents or whether or how they were being transferred.

In addition, there were no uniform safety standards or entities that were performing these transfers. As a result, congress passed Section 511 of the anti-terrorism and affected Death Penalty Act in 1996, which directed the secretary of health and human services to establish a list of biological agents and toxins that have the potential to post a serious threat to public health and safety. It also required HHS to establish, through regulation, procedures for the transfer of those agents including, among other things, ensuring that those entities have the appropriate training and skills to handle those agents safely and that entities have the proper laboratory facilities to contain and dispose of those agents.

Slide three: The Centers for Disease Control and Prevention or CDC was delegated by HHS the responsibilities for promulgating and implementing the regulation. The regulation became known officially of Section 72.6 of Title 42 of the Federal Code of Regulations and is titled Additional Requirements for Facilities Transferring or Receiving Select Agents. This

section was added to an existing CDC regulation that set minimum packaging and labeling requirements for interstate shipment of etiologic agents.

Slide four: Fundamental components of the regulations were: one, a list of 38 biological agents and toxins were listed in appendix A of Part 72. I'd like to mention that a current list of the Select Agents was also posted as one of the handouts for you to download prior to the presentation. This list is also available at the CDC Select Agent Program Web site, as shown on slide 44.

The regulation also required registration of facilities that intend to transfer these agents. It requires that each entity designate a responsible official who is required to certify that the entity meets the requirements for safe handling of these agents. The regulation further addressed transfer requirements and established a procedure for the reporting of transfers. There's a verification procedure for the regulation that involve the inspection of registered entities and, upon termination of use, the agent must be destroyed on site. This regulation contained a few or contained an opportunity to write some specific research and clinical exemptions.

Slide five: All this changed based on the terrorism events of 9/11 and the anthrax events in October of 2001. Congress quickly strengthened the anti-terrorism legislation.

Slide six: The first legislation task was the US Patriot Act. One section of that Act defined the term “restricted person”. If an individual meets the definition of a restricted person, that individual cannot have access to select agents or toxin.

Slide seven: The Public Health Security and Bio Terrorism Preparedness Response Act in 2002 was signed by President Bush on June 12, 2002. This act authorized the regulation of not only the transfer, but also the possession and use of select agents and toxins. Title 2 sub-part A of this Act significantly changed the regulatory authorities of HHS under Section 511 of the 1996 Anti-Terrorism Act. Sub-Part B of the Act granted comparable regulatory authority to the Department of Agriculture or USDA for biological agents and toxins that present a severe threat to plant and animal health or to plant and animal products. It also required USDA and HHS to coordinate activities in regard to those agents that would be regulated by both agencies. These agencies are referred to as overlap agents, which are somatic agents that have the potential to cause a severe

threat to public health and safety as well as animal health.

Slide number eight: I mentioned earlier that the statute required that several activities be coordinated with USDA. Specifically, in regards to overlap agents, the statute gives the public the opportunity to submit their application to either agency. Therefore, the entity has the choice of submitting an application for an overlap agent to either USDA or HHS. These two agencies are required to coordinate the review of the registration application. Entities with overlap select agents and toxins require concurrence of the other agency regardless of where the application is sent.

Slide nine: Some of the significant changes in the legislation are the requirements that entities, that possess these agents, would need to be registered. The original '96 legislations dealt solely with entities that intended to transfer the regulation. So this is a very important distinction between the two major pieces of legislation. In addition, the new legislation also required the establishment of safety and security requirements for entities working with these agents. As part of the security requirements, the attorney general is required to perform an electronic data check on the entity, the owner, or controller of the entity

and those individuals identified by the entity as needing access to those select agents on either the HHS or USDA regulations. This security requirement had become known as a security risk assessment and is performed by the Federal Bureau of Investigation, Criminal Justice Information Services Division or what we commonly referred to as CJIS. The Security Risk Assessment is primarily for the purpose of identifying whether individuals meet one of the prohibitors specified under the U.S. Patriot Act. The Act specifically mandates that exemptions are authorized and narrow the exemptions that were to be allowed under the old regulation.

The Act added provisions to allow the federal government to protect sensitive and site-specific information and it strengthened the criminal penalties that could be levied for violation of the Act. In addition, there is a requirement for the entity to immediately notify either USDA or HHS of the theft, loss or release of any of these agents and the requirement, on the federal government's part, to handle a report and a notification of theft, loss or release to congress. The Act also required an initial reporting of the possession of select agents and toxins.

Slide ten: On December 9, 2002, the interim final rule was on display for

the public and was later published in the Federal Register on December 13th of that year. The new regulation is titled *Possession, Use and Transfer of Select Agents and Toxins* is found in Title 42, Part 73 in the code of Federal regulations. A provision of the Act allowed for the phasing in of the implementation so that ongoing research and educational activities would not be impeded. For example, the new security requirements require developing and implementing a security plan and going through the security risk assessment process. Full implementation was required under the interim final rule on November 12, 2003.

Slide 11: One of the tasks of our interagency workgroup was to update the list of agents and toxins.

Slide 12: The establishment of select agents and toxins was a work of the interagency workgroup that I mentioned earlier. The workgroup considered the following factors when placing an agent or toxin on the final Select Agent list. They considered the effects that the agent or toxin would have on human and animal health, degree of contagiousness, mode of transmission and if there were any adequate vaccine or therapies available for the agent. In addition to input from the interagency workgroup, comments were also sought through publication of a notice in

the Federal Register.

Slide 13: As you can see here, beside some deletions and a few additions, the list did not significantly change compared to the original list published in Section 72.6. However, there were some clarifications, most notably for variola viruses, botulinum neurotoxin and Shiga toxins.

Slide 14: In 2002, legislation established the authority to create three lists of agents: those agents that are solely regulated by HHS, those that are regulated only by USDA, and those that are jointly regulated by both departments, which are referred to as overlap agents.

Slide 15: This slide shows the agents, the viruses, bacteria, fungus and toxins that are regulated by each of the two agencies. There are 20 HHS-only agents, 19 overlap agents, and 33 agents or toxins that are regulated solely by USDA.

Slide 16: Under the old regulation, there was a research exemption for toxins based only on the potency of the toxin. The interagency workgroup was tasked with reviewing this exemption and making recommendations for improvements.

Slide 17: The interagency workgroup recommended that the exemption be based not only on the potency of the toxin, but also the amount of toxin any researcher would be allowed to possess. The intent of this recommendation was to base the exemption on public health concerns and not concerns of whether this would be misused to harm one or two individuals, but if the toxin could be used to harm a large number of individuals. The threshold amount was structured such that if an individual responsible for the control of that toxin possessed less than the threshold amount, then it would be excluded from the requirements of the regulation.

Slide 18: This slide shows information from the new regulation, including the amount of toxin and the potency of the toxin. It applies only to the aggregate amount of toxin under the control of a principle investigator not necessarily the amount listed here. The CDC did not want to regulate every dermatologist who might have small quantity of botoxin for use in their office.

Slide 19: The interagency workgroup also provided recommendations on updating the genetic elements recombinant nucleic acids and recombinant

organisms section of the regulation.

Slide 20: Recommendations were to regulate genetic elements from the listed viruses that were in a host system or vector that is capable of producing a live virus. Genetic elements that encode for a functional form of any of the listed toxins would also be regulated provided that the genetic element is in a vector or host system. The intent of this regulation was to recognize the risk and concern for those individuals working with a viable agent, but not with the extracted nucleic acids, unless the nucleic acid was placed back into a system that would allow for the replication of complement forms of the select agent viruses or the potential expression of a functional form of the listed toxin.

Slide 21: The Office of Biotechnology Activity at the NIH has expressed concern over two types of experiments described in the NIH recombinant guidelines. Under these guidelines, entities receiving federal funds are prohibited from performing these experiments until they receive NIH approval. However, if an entity was not receiving federal funds, they were not required to follow the guidelines. NIH has proposed the adoption of the language of their recombinant guidelines into the new Select Agent Rule. Now, any entity that intends to work with the select

agent that meets one of these two restricted experiment provisions is required under the Select Agent Rule to receive federal government approval through the Select Agent Program before these experiments can be conducted.

Slide 22: The interagency workgroup also provided recommendations on exclusions from the regulation. I will now review the exclusions and exemption provisions of the interim final rule.

Slide 23: The select agent or toxin maybe excluded from the regulation if it is in a form or, in the case of toxins, in an amount that no longer meets the definition under the statute of posing a severe threat to public health and safety. For example, select agents and toxins in their naturally occurring environment, such as ricin in the castor bean, can be excluded from the regulation and the less the ricin is extracted from the castor bean. The new rule also recognizes that organisms that have been treated so that they are no longer able to replicate, such as treatment by gamma radiation or other appropriate means in which the organism has been rendered non-viable, are not subject to Select Agent Rule. Likewise, toxins that have been rendered non-functional are not subject to the Select Agent Rule. You are not required to register if the aggregate amount of the toxin under

control of the principle investigator is below the specific amounts shown in the regulation.

Slide 24: The new rule allows the government to exclude attenuated strains of select agents from the requirements of the regulation. Some excluded strains were published on December 13, 2002 along with the interim final rule.

Additional requests or exclusions have been received, and after the review of those requests, if the attenuated strains of the select agents were determined not to pose a severe threat to public health and safety, those excluded attenuated strains are posted on both the CDC and USDA Select Agent Web sites.

Slide 25: Several exemptions to this Act were mandated by congress. They included exemptions for clinical and diagnostic laboratories performing diagnosis, verification or proficiency testing, and products that have been approved for use by a Federal Act such as FDA. Exemptions may also be allowed for investigational products, as needed, to respond to a public health or agricultural emergency. CDC Form 1317 issues to request such exemption.

Slide 26: Under the new rule, the same fundamental principles were adopted as described under the older rule. However, the new rule requires registration for possession of select agents or toxins in addition to intent to transfer those agents or toxins. Again, the new rule adopted the provision of having the entity identify a single point of contact to represent the entity, which we refer to as the responsible official or RO. The Act requires that the entity, the owner, the responsible official and individuals who need access to these agents and toxins undergo a security risk assessment conducted by the FBI. Transfers must now be approved in advance using a CDC Form EA101, and the entity must develop and implement site-specific safety and security plans.

The entity must maintain accountability for various types of records. Some of the records that need to maintain include an inventory of the select agents or toxins, an inventory of who has access to the select agents and toxins, who has a list of people who have access to the areas where select agents and toxins are stored, and transfer documents with the transfer between entities and within the registered entity. Entities must establish emergency response plans and report theft, loss and release of any select agent or toxin. The entity is also required to conduct safety and

security training.

Slide 28: Guidance and references for developing your safety plan come from the BMBL Fourth Edition. Guidance on handling of toxins comes from OSHA, and guidance on recombinant select agents is on the guidance that's available from the NIH. The exact references for this guidance are shown on the slide.

Slide 29: Guidance with development of your laboratory security plan was published in the MMWR on December 6, 2002.

Slide 30: The regulation requires that an entity allow access to select agents and toxins only to individuals that have an approved security risk assessment. Access means the ability to gain possession of a select agent or toxin. In other words, if you are able to get your hands on a select agent or toxin, you have access to that agent or toxin, and you are required to have a security risk assessment performed prior to that access.

Slide 31: The interim final rule provides two mechanisms to prevent access. The first is a physical barrier. You can lock the door and you can lock the container, such as refrigerator or freezer where the agent is

stored; that provides a physical barrier. The second mechanism to prevent access is by the allowance of someone who already has authorization from the entity and has received security risk assessment approval to escort another person into the area. The authorized individual must be present at all times and serve as a barrier preventing the unauthorized person, for example the maintenance for cleaning personnel, from having access to the select agent or toxin.

Slide 32: A current list of persons with an approved SRA must be maintained. In addition, access in and out of areas where select agents are used or stored must be documented.

Slide 33: An inventory of select agents and toxins must be maintained at all times. Copies of all transfer documents must also be maintained.

Slide 34: In the Act, the attorney general was delegated the responsibility for performing the security risk assessments or electronic database checks, while the Department of Justice, FBI - Criminal Justice Information Services Division was identified of having responsibility for implementing this provision, and performing these database checks and providing the information. Depending on the lead agency, they would

provide this information back to either HHS or CDC or to USDA.

Slide 35: There are a few categories of individuals who are prohibited from having access to select agents. These are individuals who have been convicted of various felons. They are persons to be known to be involved with domestic or international terrorism or with organizations associated with terrorist events, would not be allowed to obtain a SRA. Persons who are agents of foreign powers are also excluded from obtaining a SRA.

Slide 36: Under the Act, the penalties for noncompliance have been strengthened and are shown on this slide. Use of penalties is a final option after other less restricted means to obtain compliance have not been successful.

Slide 37: A number of entities registered with CDC and APHIS or USDA is shown on this slide. Eighty-two percent of the entities are registered with the CDC Select Agent Program.

Slide 38: This slide shows the type of agent or toxin entities are registered for. Ninety-one percent of all entities have overlap agents or toxins.

Slide 39: When we look at just the CDC led entities, 30% of those entities are state and local public health laboratories. Another 29% or 30% are academic laboratories, and others include government, commercial and private laboratories.

Slide 40 show the types of agents associated with the CDC-led entities. About half the CDC-led entities have HHS only and overlap agents or toxins.

Slide 41: I'm sure you can see why it's very important that the CDC and USDA coordinate their efforts to implement the Select Agent Program. The registration and inspection processes only require dealing with a single designated lead agency.

Slide 42: In summary, the CDC Select Agent Program works closely with the Department of Justice, FBI, and with the Department of Agriculture, Animal and Plant Health Inspection Services. Each agency has a different role and approach to their responsibilities to implement this program.

Slide 43: During the next year, the Select Agent Program will be making some changes. We are working on a Web-based registration and

amendment process that should make submitting the forms easier for both entities regulated by CDC and USDA. The focus will be on helping entities comply now that the first round of compliance inspections have been completed. We have tasked the contractor to obtain input from entities that will be used to streamline and simplify the process of compliance. Your input will be important as we move forward with this effort.

Slide 44: This slide is a list of the Select Agent Program contacts for the various agencies involved. If you have any questions, feel free to contact, call these numbers or check the Web sites that have been listed on the slide.

Slide 45: If we have a little bit of time, I'd be happy to take some questions, but I would first like to acknowledge Mr. Mark Hemphill, Policy Director for the CDC Select Agent Program, and Dr. Leann Thomas, Director of the USDA Select Agent Program, for their assistance and their input into today's presentation. Thank you.

S. Shiflett

Thank you, Dr. Brokoff. We will now take your questions.

While we were waiting for questions, Dr. Brokoff, I have a question for you. What is the relationship between the Select Agent Program and the CDC Import Permit Program?

Dr. Brokoff That's a very good question. We've received several inquiries recently about the import programs that CDC and USDA have.

The CDC actually is operating under a regulation that requires anyone importing into the United States any etiologic agent or an arthropod, or animal host, or vector of human disease, obtain a permit from the director of CDC prior to that import. In reality, however, that does not happen.

At the present time, we do have an import program that is being managed closely with the Select Agent Program. The CDC program in reality, however, does require imports for certain types of animals, such as live bats. Import permits are required for nonhuman primate skins and tissues and also require the CDC permit.

Coordinator We currently have a question from the Nebraska Public Health Lab.

M I'd like to know why the Hantavirus and Yellow fever were deleted from

the select agent list?

Dr. Brokoff I guess, I would have to pass to Paul—I do not have an answer to that question. That happened prior to my arrival here at CDC and that's one I haven't been asked before. If you would make a note of that or submit it, we'll get you an answer and get it back to you as a result of this conference.

M Thanks.

Coordinator Our next question comes from the State Laboratory Division.

R. Sciulli This Rebecca Sciulli from the Hawaii State Lab. My question is, if a clinical laboratory has isolated a specimen that was identified by CDC as brucella melitensis and the clinical laboratory destroyed all the original specimens and the isolate, are they required to submit an EA101 to the CDC?

Dr. Brokoff Yes. The clinical lab would be required to submit, not an EA101 because you destroyed it, but you would be required to submit – it's a form called 1318, which is the report of an isolation by a clinical laboratory. On that

form, you would indicate that you have destroyed the organism after it was released or after it was identified.

R. Sciulli Thank you.

Coordinator Our next question comes from the Department of Health Main Maryland.

W Hi. This is regarding sharing information, biological agent registry information with local jurisdictions. That is, what eligible agent is in their specific county?

Dr. Brokoff I'm not sure I understand what you're asking.

W To rephrase it, to let the county know what agents one of their facilities might have in case of a first responder, a fire, what have you?

Dr. Brokoff The information that's reported to the Select Agent Program is held pretty tight to our chest. The information is not made available to others outside the program to the degree that you could identify an entity by name or location, or the organisms or toxins that might be found within that entity. So that information is not, I say readily available for purposes like that.

W Thank you.

Coordinator Next question comes from Colorado Department of Public Health.

J. Beebe This is Jim Beebe, Laboratory Services Division. For applicants for Select Agent certification, if they do not have any select agents, but merely use the checklist in the application to indicate that they want to obtain the agents, will they be certificated for them even if they don't list them on their inventory?

Dr. Brokoff Good question, Jim. If the entity is going to be registered for some of the select agents, but you want to indicate on their application that you would like to receive some of the others, that entity would go through an inspection process and could be registered.

J. Beebe So the entity would, let's say, has three agents that does not possess yet, it would be basically certificated for those agents even though it doesn't have them yet.

Dr. Brokoff Most likely we would be able to do that, Jim.

J. Beebe Thank you.

Coordinator Our next question comes from the Public Health Department in Chicago, Illinois.

T. Oldfield This is Terry Oldfield. I've been wondering if it could possibly review the notification procedures for laboratories that discover a clinical sample that they may have a select agent in?

Dr. Brokoff If a clinical laboratory—are you talking about the clinical laboratory that might isolate one of these agents? If a clinical laboratory isolates a select agent or identifies one of these toxins, that laboratory is required to obtain and complete what we refer to a CDC Form 1318. That form describes the source of the agent, the amount identified and how that agent is going to be disposed of a clinical laboratory and ship that to—a clinical laboratory that is not a registered entity can either destroy the material on site or they can ship that to a registered entity. If they plan on shipping it to a registered entity such as their public health lab or to some other laboratory, then an EA101 form would have to be completed prior to the shipment of that organism, agent or toxin to another entity.

Coordinator The next question comes from the Tennessee Department of Public Health.

D. Brown Yes. This is Diane Brown. When an entity receives an overlap agent, could you review the process of acknowledgment?

Dr. Brokoff If an entity has requested or receives an overlap agent, the form EA101 should accompany the form. That form needs to be completed and then submitted to the lead agency. If the receiving entity uses USDA as the lead agency, the form would be either e-mailed or faxed to USDA. If CDC is the lead agency for the receiving entity, the form would come here to CDC.

Coordinator Our next question comes from the Minnesota Department of Health.

W Yes. This is a follow up to your answer about a clinical laboratory isolating a select agent. If they have identified it as a select agent and then subsequently transfer it to the state department of health, you said they needed to do that using an EA101. However, the EA101 requires that both the recipient and the sender be registered laboratories and, in this

case, a clinical laboratory would not be a registered select agent laboratory. I think we've gone around about that a number of times with questions about that. Can you clarify that please?

Dr. Brokoff Let me take a crack at clarifying that for you. If the clinical laboratory submits that organism to the public health laboratory and they simply call it a clinical specimen, then they would not have to be a registered entity. In some cases, that is the way that clinical laboratories could have gotten around becoming registered in and that is acceptable to us.

Coordinator Thank you. Our next question comes from the Arizona State Laboratory.

G. Cage This is Gary Cage. We live in an endemic area for coccidioides and we see this constantly. We're just kind of curious as to why cocci is on the list and the others like histo are not.

Dr. Brokoff Gary, that's something I cannot answer. I know there were some thought given to some of these other agents, but that's something that the interagency workgroup will probably consider again.

Coordinator Our next question comes from the Wisconsin State Lab.

D. Warshauer This is Dave Warshauer. You mentioned that nonviable select agent organisms are exempt. Is it possible for a select agent lab to, say, take a gram stain or a formalinized killed organism to another lab for training purposes?

Dr. Brokoff Yes. It would be, Dave.

D. Warshauer Thank you.

Coordinator Thank you. At the moment, I currently show no further questions.

S. Shiflett Okay. Well I think that's good for the day. At this time, I think we have actually run out of time for questions. So if you do have a question and it hasn't been answered, please e-mail your questions to neoffice—that's for the Northeast Office—@nlpn.org. Dr. Brokoff will then answer your questions by an e-mail. Again, that e-mail address is neoffice@nlpn.org.

Again, I would like to remind all the participants listening to our program today to register and complete an evaluation form by November 20th. The directions for this are on your confirmation letter and in the general

handout. They were also e-mailed to each site representative this morning. Documenting your participation help us to continue to bring high quality training programs in a variety of formats. When you've completed the registration and evaluation form, you will be able to print out your CEU certificate. That concludes our program for today.

Our next teleconference will be on November 17th; the topic will be Veterinary Diagnostic Laboratory. The co-sponsors of today's program would like to thank our speakers, Dr. Charles Brokoff from the Michigan Department of Community Health in Lansing, Michigan. This is Susan Shiflett. Have a good day.